



**eunethta**  
EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT

EUnetHTA Joint Action 3 WP5A

**Guidance Document**

**EUnetHTA MULTI-HTA EARLY DIALOGUES FOR MEDICAL DEVICES**

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## Abbreviations and Definitions

D/D+/~D+: Day

DOICU: EUnetHTA Declaration of Interest and Confidentiality Undertaking.

ED: Early Dialogue

EDC: Early Dialogue Committee

EDMD: Early Dialogue for Medical Devices

EDMD WP: Early Dialogue for Medical Devices Working Party

External Experts: This group currently includes patients/patients representatives and health care professionals

EUnetHTA: European Network for Health Technology Assessment

F2F: Face to Face; Reference to a physical meeting between HTA bodies, external experts (where applicable) and the Applicant

HAS: Haute Autorité de Santé

HCP: Health Care Professional

HTA: Health Technology Assessment

HTAB/HTABs: HTA Body/Bodies

JA3: Joint Action 3

Lol: List of Issues

MD: Medical Device

Pivotal Trial: A trial that aims to assess added benefit of the medical device versus standard of care

TC: Teleconference

R: Rapporteur

SC: Scientific Coordinator

SEED: Shaping European Early Dialogues for health technologies

WP5: Work Package 5

## 1 Introduction

The European Network for Health technology Assessment (EUnetHTA) was established to create an effective and sustainable network for HTA across Europe – working together to develop reliable, timely, transparent and transferable information to contribute to HTA in European countries, creating a sustainable system of HTA knowledge sharing, and promoting good practice in HTA methods and processes. EUnetHTA Joint Action 3 (EUnetHTA JA3) aims to define and implement a sustainable model for the scientific and technical cooperation on HTA in Europe, and is co-funded by the European Commission (EC).

Within EUnetHTA JA3, Work Package 5 (WP5) aims to bridge the gaps between patients, caregivers, technology developers, current registry holders, and authorities in the health care sector, HTA producers and HTA users. Its main objective is to help to generate, all along the technology lifecycle, optimal and robust evidence for different stakeholders, bringing benefits for patient access and public health.

Multi-HTA Early Dialogues (ED) were conducted previously within the framework of EUnetHTA Joint Action 2. Additionally, between 2013 and 2015, under the coordination of Haute Autorité de Santé (HAS), France, 14 HTA Bodies (HTAB) took part in the Shaping European Early Dialogues for health technologies (SEED) project. Financed by the EC, the SEED project aimed to perform 10 Early Dialogues and explore possible scenarios for conducting Early Dialogues (ED) in the future. These EDs targeted both pharmaceutical products (8) and medical devices (2).

In the framework of EUnetHTA JA3, Multi-HTA EDs for pharmaceutical products were launched in early 2017 followed by the launch of Parallel Consultations (EDs performed in collaboration by European HTAB and the European Medicines Agency).

After a public consultation on the procedure and the briefing book template in July 2018 and a pilot ED for a medical device that concluded in November 2018, EUnetHTA is now ready to officially launch its Multi-HTA ED programme for Medical Devices.

For all submitted requests, the EUnetHTA ED Secretariat facilitates centralised HTA recruitment, and selection criteria are applied by the EDMD Working Party (EDMD WP) in order to decide if the product will be retained for an ED. The EDMD WP selection criteria and the ED process are fully explained below in [2.3 and 4 respectively](#). They also benefit from EUnetHTA ED Secretariat scientific and administrative coordination.

This guidance highlights ideal timelines and steps of procedures, rules and roles of various participants and actions for each party undertaking a Multi-HTA Early Dialogue for Medical Devices.

Further updates to this guidance are expected based on continuing experience and feedback from all participating experts.



## 2 General Principles and Rules of EUnetHTA Early Dialogues on Medical Devices

### 2.1 Principles

This guidance outlines the ideal timelines and actions for each party participating in a EUnetHTA Multi-HTA ED for a Medical Device (MD). EUnetHTA WP5 defines an Early Dialogue as non-binding scientific advice, before the start of the pivotal clinical trial (after feasibility/Proof of Concept study), in order to improve the quality and appropriateness of the data produced by the developers in view of future HTA assessment or reassessment

The advice given during a EUnetHTA Multi-HTA ED for medical devices (EUnetHTA Multi-HTA EDMD):

- ▶▶ Provides for both common advice (where the participating HTABs are in agreement) but also allows room for individual HTAB positions;
- ▶▶ Is based on the global evidence generation plan submitted by the Applicant in the EDMD Application and is valid only within this context;
- ▶▶ Is non-binding both for HTABs and for Applicants as recommendations are based on the state of science at the time the advice is given;
- ▶▶ Does not predetermine the outcome of the assessment performed later by the individual HTA agencies on that technology.

The following principles should be taken into account by Applicants willing to submit an ED request:

- ▶▶ An EDMD should be requested “early” in the product development cycle and must be submitted prior to the start of the pivotal trial to ensure that recommendations can be applied.
- ▶▶ The “early” nature of an ED does not prevent the company from submitting a detailed plan concerning the choice of population, outcomes, comparator for the pivotal trial as well and for any study they submit;
- ▶▶ EUnetHTA EDs are not intended to be iterative in nature;
- ▶▶ External experts (patients, healthcare providers/clinical experts) will be engaged by EUnetHTA as often as necessary to contribute to the ED process.

### 2.2 Scope

The process described herein is only applicable to EUnetHTA Multi-HTA EDMD.

The scope of an ED is global evidence generation and should always include the clinical development plan for the MD submitted as well as the pivotal trial (discussion about feasibility studies will not be carried out). Economic studies and discussion relative to device adoption (e.g. issues that may impede a product’s adoption in real practice) may be addressed in addition to the clinical development discussion. The Applicant chooses the areas to be discussed during the ED. An ED is requested for one indication. In certain cases, two lines of treatment or two indications could be considered for discussion.

The Applicant can only request one meeting for the same technology. Please refer to the Briefing Book Template for Medical Devices for more guidance regarding the questions to be addressed in an ED.

A EUnetHTA Multi-HTA EDMD can be held before or after technology obtains CE marking, however the ED should definitely be requested prior to the start of the pivotal trial.

### 2.3 Eligibility Criteria for an Early Dialogue on a Medical Device

EUnetHTA Multi-HTA EDMDs are restricted to MDs classified as class IIb and III, in vitro diagnostic, equipment and digital healthcare solutions/connected devices and will be selected for an ED after measurement against the EUnetHTA selection criteria:

- ▶▶ Unmet medical need;
- ▶▶ First in class;
- ▶▶ Potential impact on patients, public health, or healthcare systems.

In addition to the above selection criteria, at least 3 HTAB must agree to participate in an ED for the request to be accepted.

### 2.4 Confidentiality and Conflicts of Interest

EUnetHTA partners are bound by the EUnetHTA code of conduct and confidentiality agreement, and operate under the EUnetHTA Policy on Access to Documents. A [EUnetHTA Declaration of Interest and Confidentiality Undertaking \(DOICU\) Form](#) is used in this procedure by all participants (including HTABs, external experts, medical editors, observers, etc.). Independence between advice and subsequent assessment should be assured by each participating HTA body.

All participants (HTABs and external experts) will have access to all documents submitted by the Applicant and to Final Consolidated HTA ED Written Recommendations given on the specific advice.

In order to maintain the confidentiality of information provided by the Applicant, the exchange of all documents during an EDMD will be done through a secure file sharing system. Should the Applicant not have internally, please contact the EUnetHTA ED Secretariat via email ([eunetha-has@has-sante.fr](mailto:eunetha-has@has-sante.fr)) to establish a link using *Sharefile*.

## 3 Actors and roles in the EDMD Procedure

The actors and roles described herein are applicable only to Early Dialogues for Medical Devices. Please refer to the [EUnetHTA website](#) for information relevant to other types of EUnetHTA ED procedures.

**Applicant (Industry):** The entity submitting the request for a Multi-HTA Early Dialogue; can be a manufacturer, an importer, a distributor of a medical device. The Applicant is responsible for:

- ▶▶ Submitting the 1<sup>st</sup> Draft of Briefing Book;
- ▶▶ Revising the Draft Briefing Book based on feedback received from the EUnetHTA ED Secretariat and submitting the Final Briefing Book;
- ▶▶ Responding in writing to the EUnetHTA List of Issues;
- ▶▶ Attending F2F meeting.

**EUnetHTA ED Secretariat:** The ED Secretariat is responsible for all practical coordination of HTAB participation in an ED as well as all management aspects of an ED. The ED Secretariat is the central contact point for all EDs, responsible for all communication with the Applicant, ED Committee and external experts. The EUnetHTA ED Secretariat is responsible for:

- ▶▶ Assessing the admissibility of Draft Briefing Books;
- ▶▶ Ensuring the practical coordination of all EDMD procedures;
- ▶▶ Acting as the unique contact point for all ED procedures, managed by HAS in France.

**Early Dialogues for Medical Devices Working Party (EDMD WP):** The working party established by EUnetHTA to ensure robust high-quality HTA outputs. Except in rare cases (i.e. product outside of HTAB remit) all EDMD WP members will systematically participate in Multi-HTA EDs on Medical Devices. Current members of the EDMD WP are: AVAILA-T (ES), HAS (FR), NICE (UK), and RER (IT). The EDMD WP will be up for renewal every two years. The primary responsibilities of the EDMD WP include:

- ▶▶ Assess submissions against the predefined Eligibility Criteria for an Early Dialogue on a Medical Device set out in [2.3](#) of this document.
- ▶▶ Provide feedback to the EUnetHTA ED Secretariat regarding procedural and template revisions.

**The Early Dialogue specific Committee (EDC):** Composed of the HTABs participating in a specific ED; includes EDMD WP members and other WP5A partners on a voluntary basis. The make-up of the EDC will fluctuate to a degree for each EUnetHTA Multi-HTA EDMD. Each HTAB participant of the EDC is responsible for:

- ▶▶ Drafting and sharing their Individual Recommendations;
- ▶▶ Participating in all meetings and steps throughout the EDMD process;
- ▶▶ Reviewing and validating EUnetHTA Final Written Recommendations.

**External Experts:** External experts may participate in the evaluation phase in order to inform the EDC on a disease condition and associated healthcare management. They may be health care professionals or patients/patient representatives. Depending on their expertise, can also give their own opinion on the development proposed. Experts may be identified either by the ED Secretariat or by the individual HTABs. They can be either patients or healthcare professionals. Please refer to [6.2](#) for more information on the involvement of external experts in EUnetHTA. The role of each participating external expert is to:

- ▶▶ Review the Briefing Book (optional, according to approach);
- ▶▶ Participate in the interview with either the local HTAB or the EDC Scientific Coordinator (depending on the approach) and answer questions on the disease and development proposal;
- ▶▶ Participate in the F2F meeting (optional, according to approach).

In addition to the above, all participating external experts:

- ▶▶ Are kept informed of the final outcome of the position of the EDC (optional, according to approach);
- ▶▶ Provide feedback regarding their participation in order to improve the process;
- ▶▶ Receive feedback regarding how their contribution was used in the EUnetHTA Final Recommendations.

**EDC Scientific Coordinator:** A member of EDC chosen among EDMD WP members; acts as Scientific Coordinator on behalf of the EDC.

- ▶▶ Consolidates the HTAB List of Issues;

- »» Chair the F2F meeting with the Applicant;
- »» Consolidates Written Recommendations.

**EDC Rapporteur:** A member of EDC chosen among EDMD WP members; supports Scientific Coordinator's role. The Rapporteur works in close collaboration with the Scientific Coordinator by:

- »» Reviewing Consolidated List of Issues;
- »» Chairs the closed pre-F2F meeting with the EDC;
- »» Co-chairing F2F meeting.

**Medical Editor:** A third-party medical editor is employed in order to insure continuity and the language quality of EUnetHTA's Final Written Recommendations. Like all other participants, the Medical Editor is required to sign the EUnetHTA DOICU. Their role consists of:

- »» English language review and editing of the EUnetHTA Final Written Recommendations;
- »» Insuring language coherence throughout the document and across all EUnetHTA Final Recommendations.

**Observers:** HTABs, European Commission representatives

- »» Receive Briefing Book;
- »» Attend F2F meeting as observers;
- »» Receive Final Consolidated HTA ED Written Recommendations.

## 4 Process

### 4.1 Overview of the Early Dialogue for Medical Device Process

The Applicant requests an ED by submitting a detailed development plan using the EUnetHTA Briefing Book Template for Medical Devices. The EDMD process can be divided into three distinct phases:

1. **Preliminary phase** of exchange based on the first draft of Briefing Book. It consists in the evaluation of admissibility and eligibility of the dossier submitted.
2. **Evaluation phase** of exchange between all participants on the dossier.
3. **Final Recommendations phase** where Applicant receives final advice on its technology.

### 4.2 Preliminary Phase

#### 4.2.1 EDMD Application Submission

The Applicant submits an application for an EDMD. The application for an ED is to be addressed by e-mail to the EUnetHTA ED Secretariat (*HAS/France*): [EUnetHTA-HAS@has-sante.fr](mailto:EUnetHTA-HAS@has-sante.fr). EDs can only be requested by manufacturers, importers and distributors of MDs.

The EDMD application is composed of:

- »» The Draft **Briefing Book** using the EUnetHTA Briefing Book for Medical Devices template sent in advance by EUnetHTA ED Secretariat. The Briefing Book summarises information as the type of the industry developing the product (macro, micro, SME), rationale for seeking

advice, name of product background information, data currently available on the product, product value proposition, phase of the development (pre-clinical, in animal, in human phase2/phase3), the proposed clinical study, proposed economic evaluation, if appropriate, and the Applicant's questions and positions. Questions should be organised according to the population, intervention, comparator, outcome, time-span and type of studies (PICOTS) categories;

- »» The **trial protocol(s)**, included as an appendix of the Briefing Book;
- »» The **investigator's brochure**, if available;
- »» A **ZIP file containing all publications and study reports** referenced in the Briefing Book.

Applicants should note that requests for EDMD are grouped in "batches". A calendar is published annually on the EUnetHTA website with the submission dates for EDMD. This allows for the EDMD WP to apply selection criteria to all products received at the same time. Requests received after the published deadline will be considered for the following month.

#### 4.2.2 Admissibility Decision

After the batch deadline has passed, the EUnetHTA ED Secretariat together with the Department responsible for the assessment of Medical Devices at HAS examines the draft briefing book(s) and decides on the admissibility of each individual submission. Together they:

- »» Evaluate the completeness of the submission provided by the Applicant;
- »» Ensure that the General Principles and rules for an Early Dialogue procedure apply. (i.e. pivotal trial and not feasibility trial). If the principles and rules for an Early Dialogue do not apply, the procedure stops;
- »» Check that the proposed development plan is clear enough or if additional information is needed;
- »» Test the request against the EUnetHTA the eligibility criteria. The request will be considered as pre-eligible if all the selection criteria are met; if not, the procedure stops.

This phase may also include "clarification" requests; the ED Secretariat may request clarifications on the dossier during this period, if needed.

#### 4.2.3 Finalising the Briefing Book

Following confirmation of admissibility and pre-eligibility from EUnetHTA ED Secretariat, the Applicant submits the Final Briefing Book (both a track changes and a "clean" version) including all annexes and references and having addressed any additional requests for clarification received from the ED Secretariat. The Final Briefing Book is sent directly to EUnetHTA ED Secretariat and, as for the submission of the initial request, it is recommended that a secure file sharing system be used.

#### 4.2.4 Final step prior to starting the ED Procedure

Upon reception of the Final Briefing Book, the EUnetHTA ED Secretariat sends the request to the EDMD WP for application of the eligibility criteria and for them to declare their interest in participating. A Scientific Coordinator and Rapporteur for the EDC will be designated from among the EDMD WP members who will participate in the ED.

The request will be considered “eligible” if a majority of EDMD WP members agree that it meets the eligibility criteria (see Section 2.3 [Eligibility Criteria for an Early Dialogue on a Medical Device](#)). If the request is “eligible” a call for participation will be circulated to other HTABs. The procedure is considered validated if a minimum of 3 HTABs confirm their interest to participate in the ED. If not, the procedure stops. The Applicant will be informed of this decision in 1 weeks’ time. In the case of an accepted ED, the Applicant will be informed of the composition of the EDC.

In parallel, EDC members express their interest/intention to including experts: patients or healthcare professionals. Recruitment of experts (for detailed information see [6.2](#)) will be undertaken either by the participating HTAB or by the EUnetHTA ED Secretariat. The ED Secretariat is in charge of analysing the DOICU document of all participants for conflicts of interest. In case of any interest declared, the EUnetHTA Conflict of Interest Committee will have the final decision regarding the person’s participation.

EUnetHTA ED Secretariat establishes the timeline for each procedure following receipt of the Final Briefing Book from the Applicant and confirmation of EDC composition. The timetable is provided to all participants (HTAB and Applicant). Meeting requests will be sent by EUnetHTA ED Secretariat shortly after a meeting date is confirmed.

### **4.3 Evaluation / Discussion Phase**

#### **4.3.1 Individual List of Issues and Draft Written Positions**

Each EDC member provides, via the EUnetHTA intranet, their Individual List of Issues and Draft Written Positions (using the template provided) for each question received from the Applicant, indicating which of the questions raise particular concerns deserving specific attention from the Applicant. Issues raised can also be unrelated to the questions.

Experts should start to be interviewed around this time. The objective is to contact them rather early in order to feed the discussion on List of Issues. European experts are interviewed by EUnetHTA ED Secretariat while national experts are interviewed by their HTABs. Please refer to the section [6.2 Involvement of External](#) for more information.

#### **4.3.2 E-meeting**

EDC Scientific Coordinator compiles the Individual List of Issues and organises an e-meeting with the EDC. The Scientific Coordinator prepares a presentation with a draft Consolidated List of Issues and related questions from the Applicant when applicable. The ED Secretariat organizes an e-meeting (1.5 – 2 hours) with the EDC and if applicable, external experts. This meeting is led by the Scientific Coordinator with the aim to:

- ▶▶ Differentiate major issues to be answered in writing and discussed during F2F vs. minor issues to be answered only in writing by the company and those which could be addressed in the Final Written Recommendations or quickly during the F2F meeting;
- ▶▶ Review common and divergent positions on each issue.

Major issues are to be discussed in priority during the F2F meeting while a short written response by the Applicant would be sufficient for minor issues.

### 4.3.3 Consolidated List of Issues

Following the e-meeting:

- ▶▶ **The Scientific Coordinator** consolidates the List of Issues (Consolidated List of Issues) and posts it on the EUnetHTA Intranet;
- ▶▶ **EUnetHTA ED Secretariat** alerts EDC and external experts (when applicable) when consolidated List of Issues is available;
- ▶▶ **EUnetHTA ED Secretariat** sends the compiled List of Issues to the Applicant.

### 4.3.4 Written answers to EDC List of Issues, slides for the F2F meeting and list of participants

The Applicant reviews EDC Consolidated List of Issues submits their written response to the EDC List of Issues together with their slides for the F2F meeting and their list of participants for the meeting. After this point, no changes or modifications can be made to the documents or to their list of participants. This is in order to guarantee appropriate time for the revision and the evaluation by HTABs.

### 4.3.5 Common Draft Written Recommendations

EDC Scientific Coordinator and Rapporteur compile Common Draft Written Recommendations and prepare slides for the pre F2F meeting with HTABs.

### 4.3.6 Pre F2F meeting (morning session)

The pre F2F meeting is a closed, preliminary discussion among HTA bodies and external experts (depending on the expert approach used, see [6.2](#)) on the morning of the F2F meeting. In some cases observers may participate.

### 4.3.7 Face to Face meeting

The F2F meeting consists of a lively discussion on major issues raised by HTABs and other questions Applicant would like to address. In any case, each question from the Applicant will be answered in writing in the final HTAB recommendations.

The F2F meeting is organised at [HAS](#) headquarters, hosted by the EUnetHTA ED Secretariat, chaired by the EDC Scientific Coordinator and co-chaired by the EDC Rapporteur.

The meeting takes place in one afternoon session (max. 3 hours) and gathers HTABs and the Applicant. One or more experts (patients and/or healthcare professionals may be invited to participate by EUnetHTA deemed necessary in light of the questions submitted by the Applicant. The F2F meeting is the time to discuss the interviews conducted. In some cases it is possible that observers will be present.

#### General principles of the F2F meeting:

- ▶▶ Exchanges are about the evidence generation plan submitted by the Applicant
- ▶▶ Exchanges take into account the data available at the date of the meeting; advice and assessment given are only valuable as of the date of the meeting;
- ▶▶ Documents not provided prior to the meeting cannot be discussed.

A consultant can participate in the meeting but a meeting will not be accepted if the consultant is the only one attending.

Conclusions are taken among HTABs bodies only and will be shared in final recommendations.

Additional experts:

Experts not mentioned in the list of participants at the F2F meeting are not authorised to attend the F2F meeting.

Should anyone attend the F2F meeting with the Applicant, they will be assimilated to the pharmaceutical company requesting the advice and not considered as a clinician.

The Applicant needs to send their list of participants for the F2F meeting at the same time as their slides, no later than 4 business days prior to the meeting date.

#### **4.4 Final Recommendations Phase**

##### **4.4.1 Common Draft Written Recommendations update**

Following the F2F meeting, EDC Scientific Coordinator updates the Common Draft Written Recommendations and alerts EDC members and external experts.

##### **4.4.2 Review of Common and Finalisation of Individual Recommendations**

EDC members review Common Recommendations and finalise their individual Recommendations.

EDC members review and propose changes (in track changes mode) to the common recommendations, finalise their individual recommendations, and post them in the ED work area, notifying the Scientific Coordinator when finished. HTABs Final Written Recommendations will be consolidated as much as possible. Individual positions will be given when there is no consensual position; they will be annexed to the Final Consolidated HTA ED Written Recommendations.

##### **4.4.3 Final Review**

The EDC Scientific Coordinator finalises (in track changes mode) the Common Draft Written Recommendations and posts the document in the ED Work Area for EDC validation (EUnetHTA Final Written Recommendations). When done, the EDC Scientific Coordinator uploads the Final Consolidated HTA ED Written Recommendations and alerts EDC and external experts and observers (if applicable) by e-mail (cc EUnetHTA ED Secretariat). Five working days are allocated for review of the consolidated part and return of comments. ED Scientific coordinator informs the EUnetHTA ED Secretariat when the document is final and ready to be sent to the medical editor.

##### **4.4.4 Medical Editor Review and Sending**

A Medical Editor intervenes for the purpose of language harmonization. Their role is limited to reviewing the English and they will not conduct rewriting the Final Consolidated HTA ED Written Recommendations. The EDC Scientific Coordinator and ED Secretariat will have a final reading of the Final Consolidated HTA ED Written Answers following its return from the medical editor and send the document to Applicant EDC, experts (if applicable) and observers as a final deliverable.

#### 4.4.5 Feedback

EUnetHTA ED Secretariat conducts feedback interview(s) with external experts regarding their participation. Applicants will receive a questionnaire to be completed and returned to the ED Secretariat within 2 weeks of reception.

## 5 Timelines of the Procedure for Medical Devices

The table below outlines the procedural timelines for a EUnetHTA EDMD. Day estimations in the left-hand column should be taken as guidelines. Due to holidays, weekends and other issues, the day number of a given step may fluctuate slightly.

**Table 1. EUnetHTA EDMD Procedure**

Day	Stage	Action
<b>PRELIMINARY PHASE</b>		
<b>D-30-(+/-)</b>	EDMD Application Submission (Draft Briefing Book and other documents)	Applicant submits an application for an EDMD. EUnetHTA ED Secretariat together with the HAS Department for the evaluation of Medical Devices confirm or not the admissibility, check if information is missing. EUnetHTA ED Secretariat confirms or not the completeness of submitted application.
<b>D0</b>	Final Briefing Book	Applicant sends the Final Briefing Book with the additional documents requested (if applicable).
<b>D15</b>	EDMD WP Decision and Creation of EDC	EDMD WP reviews the Final Briefing Book against EUnetHTA Eligibility Criteria and expresses interest in participating; If the request is “eligible” it will be circulated to other HTABs. An ED request is accepted if at least 3 HTABs agree to participate. EDC is formed with EDMD WP members and any other HTABs who volunteer to participate. Each HTAB provides the names and roles of their participants. Recruitment of external experts can begin at this stage.
<b>EVALUATION PHASE</b>		
<b>D50</b>	Individual List of Issues + Draft Written Positions	Each EDC member shares Lol & Draft Written Positions (following the template) on the Intranet. EDC Scientific Coordinator, EDC members, and EUnetHTA ED Secretariat start conducting interviews with experts according to expert approach used.

<b>D55</b>	E-meeting	EDC Scientific Coordinator presents compiled Lol with distinction between major / minor comments for discussion among EDC.
<b>D70</b>	Consolidated List of Issues	EDC Scientific Coordinator consolidates the Lol; EUnetHTA ED Secretariat sends them to Applicant.
<b>D85</b>	Applicant's written response to the List of Issues + F2F meeting slides and list of participants	Sent by the Applicant to EUnetHTA ED Secretariat.
<b>D90-95</b>	Updated EDC individual draft written positions	Each EDC member shares their updated positions following the applicant's written response to the List of Issues
<b>D100</b>	Draft 1 of Common Written Recommendations	EDC Scientific Coordinator and Rapporteur compile Common Draft Written Recommendations + slides for pre F2F meeting with HTABs.
<b>D100</b>	Pre F2F meeting (morning session) + F2F (afternoon session)	Pre F2F meeting chaired by the Rapporteur and co-chaired by the EDC Scientific Coordinator. F2F meeting chaired by the EDC Scientific Coordinator and co-chaired by the Rapporteur.
<b>FINAL RECOMMENDATION PHASE</b>		
<b>D115</b>	Draft 2 of Common Written Recommendations	EDC Scientific Coordinator updates the Common Draft Written Recommendations and alerts EUnetHTA Secretariat, EDC members and external experts
<b>D120</b>	Draft 3 of Common Recommendations and individual positions	EDC members review common recommendations and finalise their individual positions.
<b>125</b>	Draft 4 of Common Recommendations and Individual Positions	EDC Scientific Coordinator reviews EDC members comments on common Recommendations and finalises this part and the inclusion of individual EDC positions in the document
<b>D130</b>	Medical Editor review of draft 4 of Common Recommendations and Individual Positions	External review by medical editor to insure language harmonisation throughout the document.
<b>D135</b>	Review and sending of Final Consolidated HTA ED Written Recommendations	Final review by EDC Scientific Coordinator / EUnetHTA Secretariat + Final Consolidated HTA ED Written Recommendations. Final pdf is sent sent to the Applicant



## 6 Practical aspects

### 6.1 Modifications of the Application

Modifications to the EDMD Briefing Book and of questions for discussion during the procedure are generally not accepted. However, if between the start of the procedure and the written responses to the EDC List of Issues the Applicant makes any changes following main issues raised through the ED process that could have a major impact on the MD development and on the related discussion (changes in the trial design or in the intended indication, new safety issues etc.) the Applicant should inform the EUnetHTA ED Secretariat about these changes as soon as possible. No changes will be accepted to the Briefing Book after reception of the Applicant's written responses to the EDC List of Issues. The EUnetHTA members reserve the right not to respond to last minute changes in the MD development.

### 6.2 Involvement of External Experts

When an eligibility decision has been made and a product has been accepted for an ED, the EUnetHTA ED Secretariat will be in charge of recruitment of external experts (patients and health care professionals). Recruitment is carried out with the support of national HTABs and European association networks for the identification of relevant experts to provide input. External experts, both patient and clinical, will be selected based on their knowledge and experience of the specific condition under study. All external experts will be required to sign a EUnetHTA DOICU prior to initiating their participation and, according to the approach used, have systematic access to the Applicant's Briefing Book.

An explanatory brochure explaining EUnetHTA Early Dialogues is sent to all participating experts.

For EUnetHTA ED, each HTAB follows their national practice for recruiting patients (Approach 1 and 2 below) and in parallel the EUnetHTA Secretariat looks to identify an EU representative (Approach 3 below).

The expert(s) will contribute punctually through an interview about the burden of the disease, current disease/patient management or similar issues. In addition, (in approach 3 described below) they can provide their own position regarding the development plan by participating in the pre-meeting with HTABs and the Face-to-Face meeting with HTABs and the Applicant.

EUnetHTA is actively involving two types of external experts in its Early Dialogue activities: Patients and Healthcare Professionals.

#### 6.2.1 Patients

For Patient involvement, three approaches are currently being tested:

- ▶ **Approach 1:** Individual patient/patient's representative;
  - interviewed regarding the disease and their experience; relevant HTAB in local language;
  - Inclusion of the participant's contribution in the final EUnetHTA recommendations;
  - Feedback questionnaire and interview with the ED Secretariat.

- ▶▶ **Approach 2:** Approach 1 + discussion with local HTAB regarding submission file (without Applicant)
  - An interview is conducted by relevant HTAB in local language;
  - The patient representative will have access to the Briefing Book;
  - Inclusion of the participant’s contribution in the final EUnetHTA recommendations;
  - Feedback questionnaire and interview with the ED Secretariat.
- ▶▶ **Approach 3:** Patient expert participating throughout the entire EDMD process
  - Approach 1 + discussion with all participating HTABs regarding the submission file and participation in the F2F meeting with the Applicant;
  - An interview is conducted by the Scientific Coordinator in English;
  - The patient representative has access to the Briefing Book, attends the e-meeting on the List of Issues and also the Face-to-Face meeting with the Applicant;
  - Inclusion of the participant’s contribution in the final EUnetHTA recommendations;
  - Feedback questionnaire and interview with the ED Secretariat.

In approaches one and two mentioned above, interviews are conducted in the local language and are translated by the interviewing HTAB into English to be shared with the EDC. For approach three, the interview is conducted in English by the Scientific Coordinator and then shared with the other EDC members. It is possible that multiple approaches could be used during the same EDMD.

### 6.2.2 Healthcare Professionals

The involvement of healthcare professionals (HCP) is similar to that of patients. An interview will be conducted by phone in the local language to address questions from the HTABs. Or in the case of an “EU Representative” expert, they will be interviewed by the Scientific Coordinator and Rapporteur. Whenever possible, EUnetHTA will invite an expert to participate in the F2F meeting.

EUnetHTA does not encourage Applicants to bring experts to the F2F meeting. In the event that this does happen, the expert will be considered at all times to be speaking on the Applicant’s behalf.

## 6.3 Medical Editing

EUnetHTA regularly solicits the outside expertise of a medical editor in order to ensure the language quality and consistency of its final recommendations. The medical editor is subject to the same rules as other experts and is obliged to submit a EUnetHTA DOICU document prior to reviewing any document.

## 6.4 Fees

The participation of HTABs in EUnetHTA EDs is currently partially covered by the EUnetHTA budget. Nevertheless, some HTABs may charge fees for their participation. Ultimately, it is up to the Applicant to decide if they accept to pay fees or not. Further information regarding fees is available upon request from the EUnetHTA ED Secretariat.

Future funding sources: to achieve the quality and sustainability of HTA Early Dialogues, the funding mechanism of these EDs will be adapted, likely by being based on a fee-for-service approach. Mechanisms for the future funding of EDs will be evaluated and decided during the last two years of JA3.

## 6.5 Contact points

The EUnetHTA ED Secretariat is the single point of contact for the Applicant and in the case of Approach 3, any external experts involved. Applicants should name a unique contact for the EUnetHTA ED exchanges.

## 6.6 Processing of documents

The ED Secretariat strongly advises Applicants to send the Briefing Book directly to the EUnetHTA ED Secretariat via a secure file-sharing system. The EUnetHTA ED Secretariat uses *Sharefile* – a secure system used by HAS for sending/ receiving documents with the Applicant. If necessary, the EUnetHTA ED Secretariat can provide a link for the Applicant to use in order to submit their EDMD Application. The EUnetHTA ED Secretariat will ensure the distribution of documents to HTABs and (if applicable) external experts involved in the procedure using the EUnetHTA intranet.

Document version control, numbering, and adherence to timelines are essential to ensure all parties have the appropriate document at the correct time.

## 6.7 Transparency rules

The EUnetHTA ED Secretariat is dedicated to transparency. In terms of the decision taken by the EDMD WP regarding the eligibility of a submission, a summary will be provided to all Applicants systematically.

Although it is recognised that the information from an early dialogue could be beneficial later in a joint assessment, EUnetHTA EDs and the final recommendations produced by the EDC are currently confidential.

## 7 Summary of Documents and Meeting Objectives

**Table 2. Description of Documents**

Document	Responsible party	Description
Draft Briefing Book	Applicant	Draft Briefing Book comprising the questions and Applicant's positions, as well all the relevant information, annexes and references, important to assess such questions. The template available on the EUnetHTA website must be used.
Requests for clarifications	EDC	Requests from EUnetHTA ED Secretariat and HAS Medical Devices Department sent to the Applicant requesting the Applicant to further clarify certain points in their Briefing Book prior to submitting the final version.
Final Briefing Book	Applicant	Finalised version of the Briefing Book addressing all points of clarification, including all annexes and references
EUnetHTA List of Issues	EDC	Document outlining the HTAB's main issues with the Applicant's proposal. Further justifications, clarification or changes to the Applicant's proposals are requested

Written response to List of Issues	Applicant	Document answering major and minor issues in written to the List of Issues raised by the EDC
Slides for F2F Meeting	Applicant	Slides should reflect the major issues raised and the answers given as well as key remaining questions that the Applicant wants to address; they do not need to restate what is in the briefing book. Template is provided by EUnetHTA ED Secretariat.
EUnetHTA Final Written Recommendations	EDC	Final Consolidated EUnetHTA written answers sent to the Applicant
Post-ED Feedback Questionnaire	Applicant	Questionnaire for applicants for EUnetHTA to gather feedback on their experience and the procedure in order to continuously improve.

**Table 3. Description of Meeting Objectives**

Meeting	Participants	Input Document	Objective of Meeting	Output Document
List of Issues e-meeting	HTAB only (experts, where applicable)	Draft positions and list of issues from each participating HTAB	The aim of the list of issues e-meeting is to: <ul style="list-style-type: none"> <li>Identify major issues on the proposed development by the Applicant;</li> <li>Identify commonalities and critical divergences between HTABs on the major aspects of trial design such as population, comparator and endpoint;</li> <li>Discuss potential solutions that could facilitate one trial, or one development plan in advance of the F2F meeting.</li> </ul>	Consolidated EUnetHTA List of Issues
Pre-F2F HTAB meeting	HTAB only (experts, where applicable)	EUnetHTA List of Issues, Written responses received from the Applicant; Expert feedback	To prepare F2F meeting: <ul style="list-style-type: none"> <li>Discuss experts input.</li> <li>Discuss changes made by the Applicant in response to EUnetHTA List of Issues;</li> <li>Review current common and diverging HTAB positions on major issues.</li> </ul>	N/A
Face to face meeting	HTAB and Applicant	Applicant's final Briefing Book	To discuss: <ul style="list-style-type: none"> <li>Main issues from</li> </ul>	EUnetHTA Final Written



(experts, where applicable)	Applicant's presentation addressing the List of Issues for discussion at face to face meeting with HTABs Any written responses from Applicant	HTABs with the Applicant's proposal regarding the major aspects of trial design. <ul style="list-style-type: none"><li>• Discuss alternatives to initial proposal.</li></ul>	Recommendations
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